Applicants: Graham P. Allaway et al.
Serial No.: 09/904,356
Filed: July 12, 2001
Exhibit 23

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JOHN P. WHITE
COOPER & DUNHAM
1185 AVENUE OF THE AMERICAS
NEW YORK, NEW YORK 10036

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	18 OCT 1996
Applicant's or agent's file reference: 43966-A-PCT	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US94/14561	16 DECEMBER 1994	17 DECEMBER 1993

Applicant
PROGENICS PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer CHRIS
Facsimile No. (703) 305-3230	Telephone

Form PCT/IPEA/416 (July 1992)*

Applicants: Graham P. Allaway et al.
Serial No.: 09/904,356
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 43966-A-PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US94/14561	International filing date *(day/month/year)* 16 DECEMBER 1994	Priority date *(day/month/year)* 17 DECEMBER 1993
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant PROGENICS PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14 JULY 1995	24 SEPTEMBER 1996
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer CHRISTINE HUCKER Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (January 1994)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US94/14561

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

[X] the international application as originally filed.

[X] the description, pages 1-46 , as originally filed.
pages NONE , filed with the demand.
pages NONE , filed with the letter of _____.
pages _____ , filed with the letter of _____.

[X] the claims, Nos. 1-19 , as originally filed.
Nos. NONE , as amended under Article 19.
Nos. NONE , filed with the demand.
Nos. NONE , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

[X] the drawings, sheets/~~fig~~ 1-4 , as originally filed.
sheets/~~fig~~ NONE , filed with the demand.
sheets/~~fig~~ NONE , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

[X] the description, pages none .
[X] the claims, Nos. none .
[X] the drawings, sheets/~~fig~~ none .

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US94/14561

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-19	YES
	Claims	none	NO
Inventive Step (IS)	Claims	none	YES
	Claims	1-19	NO
Industrial Applicability (IA)	Claims	1-19	YES
	Claims	none	NO

2. CITATIONS AND EXPLANATIONS

(See Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(6): C12Q 1/02, 1/70; G01N 21/17, 33/53 and US Cl.: 435/5, 7.1, 7.2, 7.21, 7.24, 29, 968, 974; 436/800; 530/350; 422/82.05, 82.08

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
Claims 1-19 meet the criteria set out in PCT Article 33(2), because the prior art does not teach the claimed invention.

Claims 1-19 lack an inventive step under PCT Article 33(3) as being obvious over Wanda et al in view of Dimitrov et al.
Wanda et al teach the basic concept of the invention: the use of multiple fluorescent dyes in a resonance energy transfer system to measure the fusion of different cell types. They also disclose the advantages of this system including the universality of the technique. See under "Introduction" on page 1297. They teach the use of a first dye which can absorb light at a given frequency and re-emit light at a different frequency. The second dye is chosen so that its excitation frequency overlaps the emitted light of the first dye. When two cell types, each labeled with a first and second dye respectively, are exposed to conditions that are conductive to cell fusion, the artisan can measure the fusion of the parent cells. Such a measurement can be done in an automated fashion. One could substitute the $gp120^+$ cells and $CD4^+$ cells of Dimitrov et al for the cells used in Wanda et al. Given the urgency within the medical community to find compounds that have efficacy for fighting HIV infection, one would use the method taught by Wanda et al and the cells of Dimitrov et al to assay for compounds which may block syncytia formation. The specific types of dyes used in the assay would be at the discretion of the artisan since dye absorption and emission characteristics are well known. A kit incorporating the necessary components to perform the method of the invention would be an obvious commercial expediency. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method taught by Wanda et al for the advantages disclosed therein with the cells taught by Dimitrov et al to study HIV infection, a widely known public health threat. It would be obvious to possess an agent that the artisan found to be useful and functional in the claimed method.

Applicant's arguments have been fully considered but are not deemed to be persuasive. The examiner and applicant appear to be in agreement that the difference between the instantly claimed methods of inhibiting fusion, assessing clinical progress of infected patients, staging infection, and determining the efficacy of a vaccine and the prior art method resides in the resonance energy transfer method. Applicant has argued the references separately asserting that each did not teach the claimed invention. The references are to be considered in combination for the reasons given in the previous Office Action.

Applicant concludes that there is no teaching in either cited reference nor a reasonable expectation of success that Dimitrov's cells could show a positive signal in Wanda's Method. This conclusion is not supported by any scientific evidence or reasoning. It is not convincing since the conditions of Wanda's demonstrated method is unchanged, merely the cellular receptors are changed. The substitution is done with known cellular receptors functioning in their natural capacity. There would be no reason to doubt that a cell sorter which is designed to differentiate between cells by fluorescent labels would not be able to detect the fluorescent labels of the prior art. Further, the newly cited Keller et al reference teaches inducing syncytia formation by viral mediated cell fusion. It should be noted that Keller et al is not relied upon in the ground of rejection rather its teachings are noted as consistent with those of the prior art relied upon and are cumulative to the knowledge of one of ordinary skill in the art at the time the invention was made. Applicant also argues that the instant invention determines the percentage resonance energy transfer value of the fused cells. Such mathematical manipulations of data cannot serve to establish the patentability of the claims and are merely one of many ways to display data and is a known process. For example, see Fig. 2 of the Keller et al reference. One would merely multiply the value obtained from N/N_0 and multiply it by 100 to read the data in "percent". Applicant argues that the reference do not teach substances that inhibit the binding of $gp120^+$ cells and $CD4^+$ cells. The reference were not relied upon *per se* for this teaching but rather the common knowledge of the importance of discovering cell fusion inhibiting compounds. Thus, for the reasons given above, the instant invention lacks an inventive step in view of Wanda et al and Dimitrov et al.

Claims 1-19 meet the criteria set out in PCT Article 33(4), because the instant invention has industrial applicability.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

---------- NEW CITATIONS ----------

none